

Presentation, Diagnosis and Management of a Pathological Fracture in a Case of McCune-Albright Syndrome: A Case report and Literature Review

Everisto Opondo MbChb, Mmed, FCS (Cosecsa), PhD*

Senior Lecturer, Department of Surgery, Jomo Kenyatta University of Agriculture and Technology, Nairobi, Kenya.

*Correspondence:

Everisto Opondo Mmed, FCS (Cosecsa), PhD, Department of Surgery, Jomo Kenyatta University of Agriculture and Technology, Nairobi, Kenya, Box 105,00202, Tel: +254 722475767.

Received: 02 September 2019; Accepted: 25 Septemebr 2019

Citation: Everisto Opondo. PPresentation, Diagnosis and Management of a Pathological Fracture in a Case of McCune-Albright Syndrome: A Case report and Literature Review. Surg Res. 2019; 1(2): 1-4.

ABSTRACT

McCune-Albright syndrome (MAS) is classically defined by the clinical triad of fibrous dysplasia of bone (FD), café-au-lait skin spots, and precocious puberty (PP). It is a very rare disease with estimated prevalence between 1/100,000 and 1/1,000,000. FD can involve a single or multiple skeletal sites and presents with a limp and occasionally, a pathologic fracture. The disease results from somatic mutations of the GNAS gene, specifically mutations in the cyclic Adeno Mono Phosphate (c AMP) regulating protein.

In this case report a 7-year-old female known to have MAS after presenting with precocious puberty at 3 years is presented. She presented with a pathological fracture of the femoral shaft after trivial trauma while playing at school.

The clinical diagnosis of MAS is usually made on clinical grounds. Plain radiographs are often sufficient to make the diagnosis of FD and biopsy of FD lesions during surgery can confirm the diagnosis. The mainstay of management of a pathological fracture in MAC is surgery with the goal being to achieve fracture healing and normal limb alignment.

Case Report

History and Physical examination

A 7 year old girl presented to me with history of a trivial fall and injury to the left thigh while playing at school. Prior to this she had been diagnosed with MAS at the age of three years having presented with precocious puberty and craniofacial lesions and lost to follow up. Initial evaluation at three years revealed no vision or hearing defects. However the abdominal ultrasound had revealed a large left ovarian cyst. The hormonal profile at the time was reported as normal.

She was noted at the age of 5 years to have developed a limping gait and sight shortening of the left lower limb. She attended school and had fairly normal developmental milestones according to the mother until when she had the fall and sustained a pathological fracture of the left femur. She was the third born in a family of three siblings who were all normal and no familial history of similar conditions was elicited. Physical examination revealed

craniomegaly and severe pain due to left femur fracture.

Radiological and Laboratory findings

Plain digital radiographs revealed a proximal femur with a typical ground glass appearance and shepherds crook deformity (Figures A & B). The shaft of the femur had a pathological fracture with bending of the proximal femur (Figure 1A). Radiographs demonstrated typical expansile lesions with endosteal scalloping and thinning of the cortex with the matrix of the intramedullary tissue demonstrating a "ground glass" appearance (Figures 1A & 1B).

The laboratory findings were as follows

Calcium: 2.3 mmol/L (2.02-2.65)

Phosphorous: 1.12 mmol/L (0.81-1.62)

Alkaline phosphatase: 2355.1 U/L (0-300)

Haemogram: Hb 13.7 g/dl, WBC (total) 12.56 x 10¹²/L(5-14.4),

Platelets 465 x 10⁹/L(150-450)

U/E/Cr: normal

TFT: free T3 4.94 pg/ml (2.02-4.43), free T4 (0.93-1.71), TSH 2.61 UIU/ML (0.27-4.20)

Growth Hormone; indeterminate/normal

Para Thyroid Hormone; 46.14 pg/ml

Estradiol; 24.45 pg/ml

Vitamin D; 27.46 ng/ml (30-100)

Histopathology results; Histology revealed sections of bone tissue with a hypocellular fibroblastic stroma.

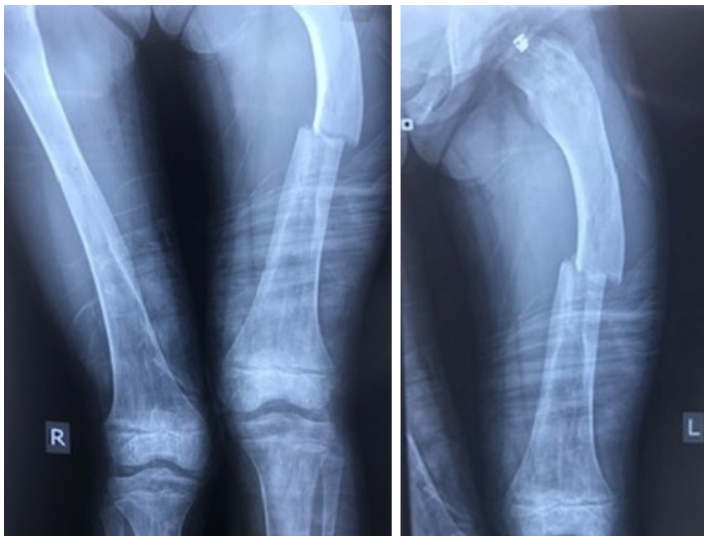


Figure 1A: Left femoral fracture with severe bow of the left femur.

Figure 1B: Left femur-showing endosteal scalloping and thinning of the cortex.



Figure 2: Picture of the femur with intramedullary titanium elastic nails post operatively.

Management

She was admitted to the Mp Shah Hospital in Nairobi and initially skin traction applied. She was reviewed by a pediatric endocrinologist and started on vitamin D 600,000 stat and calcium supplements of 250 mg. The parents were counseled about the treatment options and consented to surgery. On 6/7/2019 she underwent intramedullary nailing of the femur using two Synthes titanium elastic nails (2.5 cm). Intra operatively the medullary cavity proximal and distal to the fracture was found to be filled with fibrous tissues that blocked advancement of the nails. Due to the blockage biopsy and curettage of the medullary cavities was done prior nail insertion (Figure 2).

Proximal advancement of the nails was also limited by the severe proximal bend of the femur. However a normal limb alignment with slight shortening was achieved (Figure 3).



Figure 3: Postoperative picture of the lower limbs showing normal alignment.

Follow up

The patient has been on follow up in the out patient clinic with minimal callus seen on the check X rays at 6 weeks.

Discussion

The McCune-Albright syndrome (MAS) is diagnosed based on the triad of polyostotic fibrous dysplasia of bone (FD), café-au-lait skin pigmentation, and precocious puberty (PP) [1-10]. MAS is a rare disease with an estimated prevalence of between 1/ 100,000 and 1/1,000,000). It is due to mutations of the GNAS gene locus that results in progressive osseous heteroplasia polyostotic fibrous dysplasia on bone and some pituitary tumors [10].

It also frequently presents with endocrine conditions, including hyperthyroidism [2], growth hormone (GH) excess, renal phosphate wasting with or without rickets/osteomalacia and Cushing syndrome in association to the original triad [6-9]. Rarely, other organ systems may be involved such as the liver, parathyroid and pancreas [6].

The FD associated with MAS can involve a single skeletal site (monostotic FD, MFD), or multiple sites (polyostotic FD, PFD) [8]. Generally, FD seems to be the most common component of MAS as in this case report. Lesions of FD can affect the bones at all stages of growth process and more commonly the proximal femur [11-13]. When affected the femur deforms with a resultant bowing

and varus deformity due to the constant muscle pull and effect of body weight on the weakened bone [13]. The shepherd's crook deformity is a characteristic feature of FD that presents with pain, limb shortening, limp and femoral neck fractures. Other common sites affected by FD include the tibia, skull and ribs, although any bone can be affected [11].

The diagnosis of MAS is usually made based on the clinical features. Plain radiography of the affected region is often sufficient to make the diagnosis of FD (Figure 1). The results of genetic analysis though useful are not of clinical value as far as the diagnosis is concerned [14]. Radioisotope bone scanning is the most sensitive tool for the detection of FD lesions, and is often useful in the initial evaluation, determination of the disease extent and prediction of functional outcome [8,15]. FD has a typical appearance on radiographs described as "ground glass." In general, lesions in the long bones have a "lytic" appearance as in this case report (Figure 1A & 1B). The lesions usually arise in the medullary cavity and expand outward replacing normal bone, which results in thinning of the cortex (Figures 1A & 1B). It is usually the metaphysis and/or the diaphysis that are involved, with sparing of the epiphysis. It is possible for any bone to be involved, but the skull base and the proximal femur are the sites most commonly involved [11,15]. Because the lesions of FD are under mineralized [15], the bones are usually "soft" and prone to deformation, as exemplified by the classic "shepherd's crook" deformity of the proximal femur (Figure 2B).

Pathological fractures are more frequent in childhood, with the highest rate occurring between 6–10 years of age like in this case. While fractures do lessen after childhood, there is a persistent rate with re-fractures reported into adulthood [13].

Medical treatment using second and third generation bisphosphonates plays a crucial role in maintaining the strength of the bone, pain relief and lowering the incidence of stress fractures in selected patients [16-19]. The surgical treatment of FD has historically been a challenge with the need for multiple repeat surgeries due to poor outcomes. The main goal of surgical treatment is to restore normal alignment of the bone and to attain normal mobility. Several surgical procedures have been used for treating femoral lesions in fibrous dysplasia, including curettage and bone grafting, valgus osteotomy, plating and hip nailing, intramedullary nailing, and cortical bone grafting depending on the age at presentation [20-25]. However, the type of intervention depends on many factors such as patient age, lesion characteristics (site, size and biological behaviour) and the presence of deformity [21].

So, in managing a pathological fracture due to FD in MAC it is paramount to provide some mechanical support by internal fixation, although disease progression cannot be altered [21]. Breck [22] reported a case of fibrous dysplasia treated with total femoral plating and hip nailing, without further fracture or subsequent implant failure. Connolly [23] and Freeman et al reported the use of osteotomies with Zickel nail fixation [24].

There are various types of internal fixation for treating shepherd's crook deformity but none of them results in perfect results [26]. Due to the fact that the deformity often spares the femoral head, a firm purchase of implant in the femoral head provides sufficient mechanical to prevent recurrence of the deformity [22-25]. If a side plate is used it should be long enough to provide adequate fixation of the mechanically deficient femur and to prevent the recurrence of deformity and implant failure. In our case initial fixation using intramedullary rods didn't yield ideal results since the femoral deformity was persistent postoperatively (Figure 2). Since various studies have showed that fibrous dysplasia possesses normal bone healing properties the use of bone grafting doesn't confer any additional benefit to achieve bone union [27].

While treating fibrous dysplasia the condition of bone and stress riser should be considered and patient should be counseled about the consequences of the surgery. Several studies report the use of intramedullary implants for fixation as a better choice in preventing the stress riser likely due to bone and implant interface on the cortex of the bone seen with extramedullary implants.

Conclusion

This case illustrates the management of pathological fractures due to FD in growing bone associated with MAC. Surgical fixation by open reduction and internal fixation though recommended is challenging but achieves good clinical outcomes with limb alignment. In the paediatric population with open physis the use of titanium elastic nails after bone marrow curettage is recommended.

Acknowledgment

To the parents for giving consent for the publication of this case report.

References

1. McCune DJ. Osteitis fibrosa cystica: the case of a nine-year-old girl who also exhibits precocious puberty, multiple pigmentation of the skin and hyperthyroidism. *Am J Dis Child.* 1936; 52: 743-744.
2. Albright F, Butler AM, Hampton AO, et al. Syndrome characterized by osteitis fibrosa disseminata, areas, of pigmentation, and endocrine dysfunction, with precocious puberty in females: report of 5 cases. *N Engl J Med.* 1937; 216: 727-746.
3. Russell LW, Chandler FA. Fibrous dysplasia of bone. *J Bone Joint Surg Am.* 1950; 32: 323-337.
4. DiCaprio MR, Enneking WF. Fibrous dysplasia. Pathophysiology, evaluation, and treatment. *J Bone Joint Surg Am.* 2005; 87: 1848-1864.
5. Danon M, Crawford JD. The McCune-Albright syndrome. *Ergeb Inn Med Kinderheilkd.* 1987; 55: 81-115.
6. Diaz A, Danon M, Crawford J. McCune-Albright syndrome and disorders due to activating mutations of GNAS1. *J Pediatr Endocrinol Metab.* 2007; 20: 853-880.
7. McCune-Albright syndrome. In *Sexual precocity: etiology, diagnosis and management* Edited by: Grave GD, Cutler GB. New York: Raven Press; 1993: 243-251.

8. Ippolito E, Bray EW, Corsi A, et al. Natural history and treatment of fibrous dysplasia of bone: a multicenter clinicopathologic study promoted by the European Pediatric Orthopaedic Society. *Journal of pediatric orthopaedics*. 2003, 12: 155-177.
9. Riminucci M, Liu B, Corsi A, et al. The histopathology of fibrous dysplasia of bone in patients with activating mutations of the Gs alpha gene: site-specific patterns and recurrent histological hallmarks. *The Journal of pathology*. 1999; 187: 249-258.
10. Alman BA, Greel DA, Wolfe HJ. Activating mutations of Gs protein in monostotic fibrous lesions of bone. *J Orthop Res*. 1996; 14: 311-315.
11. DiCaprio MR, Enneking WF. Fibrous dysplasia. Pathophysiology, evaluation, and treatment. *J Bone Joint Surg Am*. 2005; 87:1848-1864.
12. Albright F, Butler AM, Hampton A, et al. Syndrome characterized by osteitis fibrosa disseminata, areas of pigmentation and endocrine dysfunction, with precocious puberty in females. *N Engl J Med*. 1937; 216: 727-746.
13. Guille JT, Kumar SJ, MacEwen GD. Fibrous dysplasia of the proximal part of the femur. Long-term results of curettage and bone-grafting and mechanical realignment. *J Bone Joint Surg Am*. 1998; 80: 648-658.
14. Lee SE, Lee EH, Park H, et al. The diagnostic utility of the GNAS mutation in patients with fibrous dysplasia: meta-analysis of 168 sporadic cases. *Hum Pathol*. 2012; 43: 1234-1242.
15. Enneking WF, Grearen PF. Fibrous dysplasia of the femoral neck. Treatment by cortical bone-grafting. *J Bone Joint Surg Am*. 1986; 68: 1415-1422.
16. Lane JM, Khan SN, O'Connor WJ, et al. Bisphosphonate therapy in fibrous dysplasia. *Clin Orthop Relat Res*. 2001; 382: 6-12.
17. Chapurlat RD, Hugueny P, Delmas PD, et al. Treatment of fibrous dysplasia of bone with intravenous pamidronate: long-term effectiveness and evaluation of predictors of response to treatment. *Bone*. 2004; 35: 235-242.
18. Liens D, Delmas PD, Meunier PJ. Long-term effects of intravenous pamidronate in fibrous dysplasia of bone. *Lancet*. 1994; 16: 343: 953-954.
19. Ozaki T, Sugihara M, Nakatsuka Y, et al. Polyostotic fibrous dysplasia: a long term follow up of 8 patients. *Int Orthop*. 1996; 20: 227-232.
20. Stanton RP. Surgery for fibrous dysplasia. *J Bone Miner Res*. 2006; 21(Suppl 2): 105-109.
21. Bernardo Vagars. *Orthopaedic surgery for Fibrous Dysplasia emedicine*. Medscape. 2016.
22. Breck LW. Treatment of fibrous dysplasia of bone by total femoral plating and hip nailing. *Clin Orthop*. 1972; 82: 82-83.
23. Connolly JF. Shepherd's crook deformity of polyostotic fibrous dysplasia treated by osteotomy and Zickel nail fixation. *Clin Orthop Relat Res*. 1977; 123: 22-24.
24. Freeman BH, Bray EW 3rd, Meyer LC. Multiple osteotomies with Zickel nail fixation for polyostotic fibrous dysplasia involving the proximal part of the femur. *J Bone Joint Surg [Am]*. 1987; 69: 691-698.
25. Guille JT, Kumar SJ, MacEwen GD. Fibrous dysplasia of the proximal part of the femur: long-term results of curettage and bone-grafting and mechanical realignment. *J Bone Joint Surg [Am]*. 1998; 80: 648-658.
26. Yamamoto T, Hashimoto Y, Mizuno K. Oblique wedge osteotomy for femoral diaphyseal deformity in fibrous dysplasia. *Clin Orthop*. 2001; 384: 245-249.
27. Campanacci M. *Fibrous dysplasia in Bone and Soft Tissue Tumors*, 2nd edition. New York: Springer-Verlag Wien. 1999; 435-461.